What Is Claimed Is:

A compound of Formula I:

in which:

A² R^{1} I

the dashed lines indicate optional unsaturation without violating valency rules;

 R^1 is hydrogen, $(C_{1.6})$ alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R¹ is absent when a double bond exists between the nitrogen atom to which R¹ is attached and an adjacent ring atom or R¹ is as defined below;

 X^1 is -NR²-, -S-, -S(O)-, -S(O)₂- or -O-, wherein R² is hydrogen or (C₁₋₆)alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom;

A1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A¹ together with R¹ and the atoms to which A¹ and R¹ are attached form\(a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A¹ may be substituted with a group selected from -X²R³, -X²QR³, -X²C(O)R³, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)_2$, R^3 , $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C₁₋₆)alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10

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ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A¹ and R⁵ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²SR⁴, -X²SR⁴, -X²SR⁶, -X²SR⁶, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²NR⁴S(O)₂R⁶ and X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A¹ and R⁵ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A¹ and R⁵ is a fused polycyclic ring system;

A² is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A² may be substituted with a group selected from $-X^2R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is X^2R^9 wherein X^2 is as defined above and R9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A² and R⁸ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^{2}NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)R^{6}$, $-X^{2}NR^{4}C(O)OR^{4}$, $-X^{2}C(O)NR^{4}R^{4}$,

50 V

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 $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{4})NR^{4}R^{4}$, $-X^{2}C(O)NR^{4}X^{2}C(O)OR^{4}$, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C_{1.6})alkyl or halo-substituted (C_{1.6})alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A2 and R8 may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A² and R⁸ is a fused polycyclic ring system; and

A³ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of oto 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from -X²R⁹, -X²OR⁹, -X²C(O)R⁹, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)QR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C_{1.5})alkyl or halo-substituted (C_{1.5})alkyl, wherein each ring within A³ and R¹⁰ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C_{1.6})alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, -X2NR4S(O)2R6 and -X2S(O)2NR4R4, wherein X2 and R4 are as defined above and R⁶ is (C_{1.6})alkyl or halo-substituted (C_{1.6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A³ and R¹⁰ may be substituted further with 1 to 2 groups independently selected from (C_{16}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A3 and R10 is a fused

polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof;

with the proviso that when said compound is selected from the group consisting of Formulae II(a), II(b) and II(c):

then A^3 is other than:

unsubstituted pyridyl;

unsubstituted thienyl;

unsubstituted indolyl;

unsubstituted phenyl;

benzo[1,3]dioxolyl;

2,3-dihydro-benzo[1,4]dioxinyl;

phenyl which is mono-substituted by fluoro, bromo, iodo, nitro, methyl, isopropyl, ethoxy or methylsulfanyl; and

phenyl which is substituted by at least one of chloro, hydroxy or methoxy.

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2. The compound of claim 1, and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts of said compound, with the further proviso that A³ is other than:

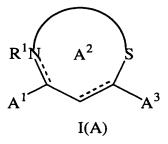
unsubstituted pyridyl; unsubstituted thienyl;

unsubstituted indolyl; unsubstituted phenyl; benzo[1,3]dioxolyl;

2,3-dihydro-benzo[1,4]dioxinyl; and

phenyl which is substituted by at least one of halogen, nitro, hydroxy, (C_1) alkyl, methoxy, ethoxy and methylsulfanyl.

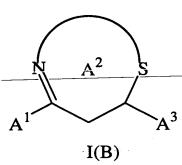
- 3. The compound of claim 1, and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts of said compound, with the further proviso that A¹ is not 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl.
- 4. The compound of Claim 1 in which said compound is of Formula I(A):



in which R¹, A¹, A² and A³ are as defined in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

5. The compound of Claim 4 in which said compound is of Formula

50h A2 **I(B)**:

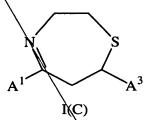


5 Jh A2

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in which R^1 , A^1 , A^2 and A^3 are defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

6. The compound of Claim 5 in which said A² is 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene, that is the compound of Formula I(C):



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in which A^1 and A^3 are defined as in Claim 1, and said 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

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The compound of Claim 6 in which A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

8. The compound of Claim 7 in which said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2\one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-tr\fluoromethylsulfanyl-phenyl)-2,3,6,7tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-triflu@romethylsulfanyl-phenyl)-2,3,6,7tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7\tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1\4]thiazepin-5yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-

yl}-4-hydroxy-6-methyl-pyran-2-one; $3-\{7\times[5-(4-\text{chloro-phenyl})-\text{furan-}2-\text{yl}\}-2,3,6,7-\text{tetrahydro-}[1,4]\text{thiazepin-}5$ yl}-4-hydroxy-6-methyl-pyran-2-one; 5 4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-[5-yl]-pyran-[2-one]3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4hydroxy-6-methyl-pyran-2-one; 3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4hydroxy-6-methyl-pyran-2, one; OSS WOLLD 15 3-[7-(1-benzenesalfonyl-1H-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; 4-hydroxy-6-methyl-3-\[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; 4-hydroxy-6-methyl-3-[7-(\subseteq-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; 4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; 3-[7-(3-chloro-2-methyl-5-trifluordmethyl-1H-pyrazol-4-yl)-2,3,6,7-20 tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; $3-\{7-[1-(2,4-difluoro-benzenesulfonyl)-1H-pyrrrol-2-yl]-2,3,6,7$ tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one; 3-(7-[2,2']bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4hydroxy-6-methyl-pyran-2-one; 25 $3-\{7-[1-(3,5-dichloro-phenyl)-1H-pyrrrol-2\yl]-2,3,6,7-tetrahydro-$ [1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one; $3-\{7-[1-(4-chloro-phenyl)-1H-pyrrrol-2-yl]-2,3,6,7-tetrahydro-$ [1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one; 3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-30 hydroxy-6-methyl-pyran-2-one;

- 4-hydroxy-6-methyl-3-[7-(6-p-tolylsulfanyl-imidazo[2,1-b]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
- 3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
- 4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
- 3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
- 3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
- 4-hydroxy-6-methyl 3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
- 3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
- 4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran 2-one; and
- 3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-methoxy-6-methyl-pyran-2-one;

and the N-oxide derivatives, produg derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

- 9. The compound of Claim 6 in which A¹ is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 10. The compound of Claim 9 in which said compound is selected from the group consisting of:

3-\[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;
3-\[7-\(2,4-\)diethoxy-phenyl\)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]=

4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-d)methylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; and

3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

- 11. The compound of Claim 6 in which A¹ is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 12. The compound of Claim 1 in which said compound is selected from the group consisting of:

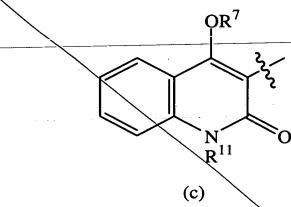
2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

 $\sqrt{3}$. The compound of claim 6 in which A¹ is a group of Formula (c):



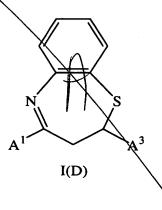
in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valence is attached to A^2 ; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

14. The compound of Claim 13 which is:

3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

15. The compound of Claim 5 in which said A^2 is 2,3-dihydrobenzo[b][1,4]thiazepin-5,7-ylene that is the compound-of Formula I(D):



in which A¹ and A³ are defined as in Claim 1, and said 2,3-dihydrobenzo[h[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C¹-6)alkyl, cyano, halo, nitro, halo-substituted (C¹-6)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²C(O)OR⁶, -X²C(O)OR⁶, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁶, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² is a bond or (C¹-6)alkylene, R⁴ at each occurrence independently is hydrogen, (C¹-6)alkyl or halo-substituted (C¹-6)alkyl, and R⁶ is (C¹-6)alkyl or halo-substituted (C¹-6)alkyl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

16. The compound of Claim 15 in which A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

17. The compound of Claim\16 which is:

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

18. The compound of Claim 15 in which A¹ is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

19. The compound of Claim 18 which is:

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

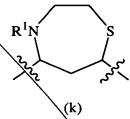
and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

- 20. The compound of Claim 15 in which A¹ is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 21. The compound of Claim 20 in which said compound is selected from the group consisting of:
- 3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone; and
- 3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

22. The compound of Claim 4 in which said A² is a group of Formula

20 5 U M A Y (k):



in which R^1 is defined as in Claim 1 and said group of Formula (k) may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2QR^4$, $-X^2C(Q)R^6$, $-X^2QC(Q)R^6$, $-X^2QQ(Q)R^6$, $-X^2QQ(Q)R^6$, $-X^2QQ(Q)R^6$, $-X^2QQ(Q)R^6$, $-X^2QQ(Q)R^6$, $-X^2QQ(Q)R^6$, $-X^2QQ(Q)Q^6$,

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 $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^4 at each occurrence independently is hydrogen, $-(C_{1-6})$ alkyl or halo-substituted (C_{1-6}) alkyl, and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

- 23. The compound of Claim 22 in which R¹ is hydrogen; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 24. The compound of Claim 22 in which A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 25. The compound of Claim 24 in which said compound is selected from the group consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl) [1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

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26. The compound of Claim 22 in which A¹ is optionally substituted phenyl.

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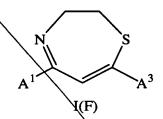
27. The compound of Claim 26 which is:

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)[1,4]thiazepan-4-yl]-ethanone;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

28. The compound of Claim 4 in which said A² is 2,3-dihydro-[1,4]thiazepin-5,7-ylene that is the compound of Formula I(F):

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in which A¹ and A³ are defined as in Claim 1, and said 2,3-dihydro[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)₂R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, wherein X² is a bond or (C₁₋₆)alkylene, R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

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29. The compound of Claim 28 in which A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

- The compound of Claim 29 in which said compound is selected from the group consisting of:
- 3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
- 3-[7-(2,4-drethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and
- 3-(7-[2,2']bithicnyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

- 31. The compound of Claim 28 in which A¹ is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
 - 32. The compound of Claim 31 which is:
- 3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

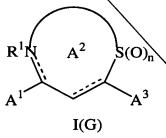
and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

33. The compound of Claim 28 in which A¹ is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone,

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

35. The compound of Claim 1 in which said compound is of Formula I(G):



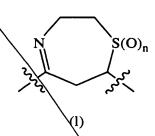
in which n, R^1 , A^1 , A^2 and A^3 are defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

36. The compound of Claim 35 in which A² is a group of Formula (1)



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in which n, and R¹ are defined as in Claim 1 and said group of Formula (l) may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, wherein X^2 is a

Sub Ak

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bond or (C_{1-6}) alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and the W-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

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37. The compound of Claim 36 in which n is 1 and A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

38. The compound of Claim 37 which is:

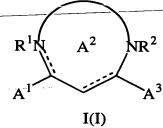
 $3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1H-1\lambda^4-[1,4]$ thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

- 39. The compound of claim 36 in which n is 2 and A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 40. The compound of claim 39 which is 3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3) 6,7-tetrahydro- $1H-1\lambda^6-[1,4]$ thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one:

and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

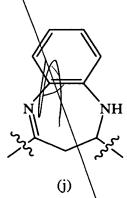
41.



in which R^1 , R^2 , A^1 , A^2 and A^3 are as defined in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

42. The compound of Claim 41 in which said A² is a group of Formula

(j):



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in which said group of Formula (j) may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and (C_{1-6}) alkyl or halo-substituted derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

43. The compound of Claim 42 in which A¹ is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

44. The compound of Claim 43 which is:

3 - [4 - (2, 4 - d i m e t h o x y - p h e n y l) - 4, 5 - d i h y d r o - 3 H - benzo[b][1,4]diazepin-2-yl]-4-hydroxy-6-methylpyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

45. The compound of Claim 1 in which said compound is of Formula I(K):

in which A³ is defined as in Claim 1; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

46. The compound of claim 45 which is:

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10H-2,5-dioxa-9-thia-6a-aza-cyclohepta[a]naphthalene-1,6-dione;

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and the N-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

	receptable saits thereof.
	47. A compound selected from the group consisting of:
_	4-hydroxy-3-17-(2-methoxy-4-methylsulfanyl-phenyl)-2.3 6.7-tetrahydro
	[1,4]tniazepin-5-yl]-6-methyl-pyran-2-one;
c 1.	3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-
SW	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
BI	3-[7-(4-dimethylamino-2 methoxy-phenyl)-2.3.6.7-tetrahydro
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
¥10	4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2.3.6.7-tetrahydro
	[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and
The T	4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7 tetrahydro-[1,4]thiazepin-5-
0 110 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	yl]-6-methyl-pyran-2-one; or
3	a N-oxide derivative, prodrug derivative, protected derivative, individual
15 	stereoisomer and mixtures of stereoisomers; or the pharmaceutically acceptable
	salt thereof.
Stanoore	48. A compound selected from the group consisting of:
	7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2 <i>H</i> -pyran-3-yl)-
	2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepine-3-carboxylic acid; and
20	$2-(\{1-[7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl, 2, organization)\}$
SUM	2H-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepin-3-yl]-methanoyl}-
A7	amino)-propionic acid tert-butyl ester;
11.	and the N-oxide derivatives, prodrug derivatives, protected derivatives;
	and the pharmaceutically acceptable salts thereof
25	49. The compound of Claim in which A ¹ is a group selected from
	Formulae (b), (c), (d), (e) and (f):

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 , or

 A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):

wherein X^1 is -S- and the free valance is attached to A^3 ; and

 A^2 is as defined above or is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-X^2R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$,

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 $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(Q)_2R^8$ and $-X^2S(Q)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is -X²R⁹ wherein X² is as defined above and R⁹ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A² and R⁸ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted ($C_{1.6}$)alkyl, X^2OR^4 , $X^2C(O)R^6$, $X^2OC(O)R^6$, $X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said heteroalkylene, carbocycloalkyl and heterocycloalkyl rings within A² and R⁸ may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A² and R⁸ is a fused polycyclic ring system; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

The compound of Claim 49 in which λ^2 is a group selected from 50. Formulae (h), (i), (j), (k), (l) and (m):

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl or A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):

wherein X^1 is -S- and the free valance is attached to A^3 ; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

51. A compound of Formula II:

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 OR^7R^1N A^2 A^3 II

in which:

the dashed lines indicate optional unsaturation without violating valency rules;

 R^1 is hydrogen, (C_{16}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

R⁷ is hydrogen;

 X^1 is -NR²-, -S-, -S(O)-, $S(O)_2$ - or -O-, wherein R² is hydrogen or (C_{1-6}) alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom;

 A^2 is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2C(O)R^8$, $-X^2C(O)R^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)R^8$, $-X^2C(O)R^8$, -

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CODUMNT OF HOCH

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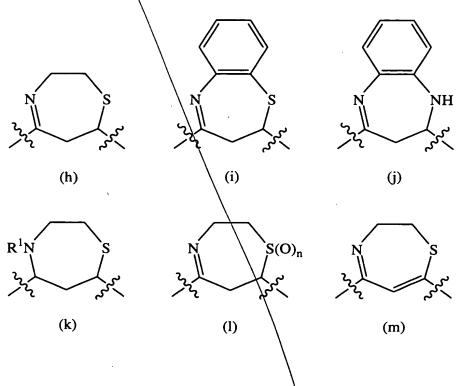
 $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said heteroalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A³ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from -R⁹, -X²OR⁹, -X²C(O)R⁹, -X²OC(O)R⁹, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^9 is -X²R¹⁰ wherein X² is as defined above and R¹⁰ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A^3 and R^{10} contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted ($C_{1.6}$)alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$ \, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^{2}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{4})NR^{4}R^{4}$, $-X^{2}NR^{4}S(O)_{2}R^{6}$ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A³ and R¹⁰ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo with

the proviso that only one of A³ and R¹⁰ is a fused polycyclic ring system; and the V-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof;

provided, however, Formula II does not represent a compound wherein A^2 is 2,3,6,7-tetrahydro-[1,4]thiazepinylene, 2,3-dihydro-benzo [b] [1,4] thiazepinylene or 7-trifluoro-2,3-dihydro-benzo [b] [1,4] thiazepinylene and A^3 is benzo [1,3] dioxolyl, indolyl, phenyl, pyridyl or thienyl, wherein said phenyl may be substituted with 1 to 3 groups independently selected from halo, nitro, hydroxy, $(C_{1,4})$ alkyl, $(C_{1,4})$ alkylsulfanyl and $(C_{1,4})$ alkyloxy or any N-oxide derivative; protected derivative, individual stereoisomer or mixture of stereoisomers, or pharmaceutically acceptable salt thereof.

52. The compound of Claim 51 in which A^2 is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



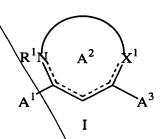
in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl or A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):

wherein X^1 is -S- and the free valance is attached to A^3 ; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

- 53. The compound of Claim 52 in which A³ is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A³ may be substituted with a group selected from -R9, -X²OR9, -X²SR9 and -X²S(O)₂R9, wherein R9 is -X²R¹0, X² is a bond or (C₁-6)alkylene and R¹0 is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A³ and R¹0 may be substituted with 1 to 3 groups independently selected from (C₁-6)alkyl, halo, halo-substituted (C₁-6)alkyl, -X²OR⁴, -X²SR⁴, -X²S(O)₂R⁶ and -X²NR⁴R⁴, wherein R⁴ at each occurrence independently is hydrogen, (C₁-6)alkyl or halo-substituted (C₁-6)alkyl and R⁶ is (C₁-6)alkyl or halo-substituted (C₁-6)alkyl; and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.
- 54. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1, 47 or 51 or a *N*-oxide derivative, prodrug derivative, individual isomer or mixture of isomers or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient.

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- 55. The pharmaceutical composition of Claim 54, further comprising at least one known cancer chemotherapeutic agent.
- 56. The pharmaceutical composition of Claim 55, wherein said cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubisin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin® Rituxan® and alanosine.
- 57. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

 R^1 is hydrogen, (C_{1-6}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

 X^1 is -NR²-, -S-, -S(O)-, -S(O)₂- or -O- wherein R² is hydrogen or (C₁₋₆)alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom;

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containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14

A¹ is a monocyclic or fused polycyclic ring system selected from aryl

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ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A¹ together with R¹ and the atoms to which A¹ and R¹ are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A¹ may be substituted with a group selected from -R³, -X²OR³, -X²C(O)R³, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, X^2SR^3 , $-X^2S(O)R^3$, $-X^2S(O)_2R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)QR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_3R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C_{1.6})alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, $(C_{1.6})$ alkyl or halo-substituted $(C_{1.6})$ alkyl, wherein each ring within A¹ and R⁵ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4, -X^2SR^4, -X^2S(O)R^6, -X^2S(O)_2R^6, \\ \Big\backslash -X^2NR^4R^4, -X^2NR^4C(O)R^6, \\ -X^2NR^4R^4, -X^2NR^4C(O)R^6, \\ -X^2NR^4R^4, -X^2NR^4R^4, \\ -X^2NR^4R^4, -X^2NR^4R^4, \\ -X^2NR^4, \\ -X^2NR^4, \\ -X^2NR^4, \\ -X^2NR^4, \\ -X^2NR^4, \\ -X^2NR^$ $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R^6 is $(C_{1.6})$ alkyl or halo-substituted $(C_{1.6})$ alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A¹ and R⁵ may be substituted further with 1 to 2 groups independently selected from $(C_{1.6})$ alkylidene, oxo, imino and thioxo, with the provisos that only one of A\ and R⁵ is a fused polycyclic ring system;

A² is a monocyclic or fused bicyclic ring selected from heteroarylene or

unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A² may be substituted with a group selected

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from -R8, -X2OR8, -X2C(O)R8, -X2OC(O)R8, -X2C(O)OR8, -X2SR8, -X2S(O)R8, $-X^{2}S(O)_{2}R^{8}$, $-X^{2}NR^{4}R^{8}$, $-X^{2}NR^{4}C(O)R^{8}$, $-X^{2}NR^{4}C(O)OR^{8}$, $-X^{2}C(O)NR^{4}R^{8}$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$. wherein X^2 is a bond or $(C_{1.6})$ alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R9 is ary containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C₁₋₆) alkyl, wherein each ring within A² and R⁸ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^{2}NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)R^{6}$, $-X^{2}NR^{4}C(O)OR^{4}$, $-X^{2}C(O)NR^{4}R^{4}$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C_{1.6})alkyl or halo-substituted (C_{1.6})alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A² and R⁸ may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the proviso that only one of A² and R⁸ is a fused polycyclic ring system; and

A³ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from -R9, -X²OR9, -X²C(O)R9, -X²OC(O)R9, -X²C(O)OR9, -X²SR9, -X²S(O)R9, -X²S(O)₂R9, -X²NR4R9, -X²NR4C(O)R9, -X²NR4C(O)OR9, -X²NR4C(O)OR9, -X²NR4C(O)NR4R9, -X²NR4C(O)NR4R9, -X²NR4C(O)NR4R9, -X²NR4C(O)R4R9, -X²NR4C(O)R4R9, -X²NR4C(O)R4R9, wherein X² is a bond or (C₁₋₆)alkylene, R9 is -X²R10 wherein X² is as defined above and R10 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated,

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partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R4 at each occurrence independently is hydrogen, (C_{1.6})alkyl or halo-substituted (C_{1.6})alkyl, wherein each ring within A³ and R¹⁰ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^{2}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{4})NR^{4}R^{4}$, $-X^{2}NR^{4}S(O)_{2}R^{6}$ and -X2S(O)2NR4R4, wherein X2 and R4 are as defined above and R6 is (C1-6)alkyl or halo-substituted $(C_{1-6})a|ky|$, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A3 and R10 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A³ and R¹⁰ is a fused polycyclic ring system; or an N-oxide derivative, prodrug \derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula $\Pi(a)$:

then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino
- 58. The method of claim 57, with the further proviso that when said compound is selected from the group consisting of Formula II(a) and II(b):

HO N S HO N S A A II(b)

- then A³ is other than:
 - (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino
- 59. The method of claim 57, with the further proviso that when said compound is selected from the group consisting of Formula II(a) and II(b):

then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) 2,3-dihydro-benzo[1,4]dioxinyl; and
- (c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C_{1-3}) alkyl.

OR^{.7.} QR⁻⁷ ŌR⁷ N R¹¹ (a) (b) (c) QR⁷ (d) (e)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A², or

 A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):

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wherein X^1 is -S- and the free valance is attached to A^3 ; and A^2 of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):

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in which n is 1 or 2 and R¹ is acetyl or trifluoroacetyl; or an N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, halo, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

	62. The method of Claim 61, wherein said compound is selected from
	the group consisting of:
	2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]
	3-hydroxy-cyclohex-2-enone;
5	4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-
- 1	[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;
5 uh	3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl]-
Bl	4-hydroxy-6-methyl-pyran-2-one;
/ / ·	3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-
10	4-hydroxy-6-methyl-5,6-dihydro-pyran 2-one;
o u	3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-
	4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;
	2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-
3	3-hydroxy-cyclohex-2-enone;
□ 15 -	3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-
ja 4	[1,4]thiazepin-5-yl]-cyclohex-2-enone;
	3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-
in the second se	benzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone;
	4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-
20	benzo[b][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one; and
	4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-
	2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; or
•	a N-oxide derivative, prodrug derivative, protected derivative, individual
2.5	stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt
25	thereof.
	

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63. The method of claim 57, wherein said compound is selected from the list consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

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3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-
                methyl-pykan-2-one;
                      3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-
               5-yl]-4-hydrox x-6-methyl-pyran-2-one;
    5
                      1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-
               [1,4]thizepan-4-yl]\ethanone;
                      4-hydroxy-6-methyl-3-[7-(3-phenyl-1H-pyrazol-4-yl)-2,3,6,7-tetrahydro-
               [1,4]thiazepin-5-yl]-pykan-2-one;
                      3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
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              hydroxy-6-methyl-pyran-2\one;
                      3-[7-(1-benzyl-1H-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
              hydroxy-6-methyl-pyran-2-ond;
                     4-hydroxy-6-methyl-3[^{1}\/-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-
              tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
                     4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-
              tetrahydro-[1,4]thiazepin-5-yl]-pyran\2-one;
                     4-hydroxy-6-methyl-3[7-(4-tr)fluoromethylsulfanyl-phenyl)-2,3,6,7-
              tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
                    4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-
  20
              tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
                    3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-
             5-yl]-4-hydroxy-6-methyl-pyran-2-one;
                    3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-
             5-yl]-4-hydroxy-6-methyl-pyran-2-one;
 25
                    4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-
             2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;
                    yl}-4-hydroxy-6-methyl-pyran-2-one;
                    3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
 30
            yl}-4-hydroxy-6-methyl-pyran-2-one;
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	3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
	yl}-4-hydroxy-6-methyl-pyran-2-one;
	4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-
	yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;
5	3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
~	hydroxy-6-methyl-pyran-2-one;
, 0)	3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
A 1 '	hydroxy-6-methyl-pyran-2-one;
	3-[7-(1-benzenesulfonyl-1H-pyrrol-2-yl)-2,3,6,7-tetrahydro-
_ 10	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
10 11 11	4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-
Li	[1,4]thiazepin-5-yl]-pyran-2-one;
	4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-
T T	[1,4]thiazepin-5-yl]-pyran-2-one;
_g 13	4-hydroxy-6-methyl-3-[7-(1-methyl-1 <i>H</i> -indol-3-yl)-2,3,6,7-tetrahydro-
-	[1,4]thiazepin-5-yl]-pyran-2-one;
	3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1 <i>H</i> -pyrazol-4-yl)-2,3,6,7-
American	tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
The Con-	3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1H-pyrrrol-2-yl]-2,3,6,7-
20	tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;
	3-(7-[2,2']bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-
	hydroxy-6-methyl-pyran-2-one;
	$3-\{7-[1-(3,5-dichloro-phenyl)-1H-pyrrrol-2-yl]-2,3,6,7-tetrahydro-$
	[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;
25	$3-\{7-[1-(4-chloro-phenyl)-1H-pyrrrol-2-yl]-2,3,6,7-tetrahydro-$
	[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;
	3-[7-(5-chloro-1H-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
	hydroxy-6-methyl-pyran-2-one;
	4-hydroxy-6-methyl-3-[7-(6- p -tolylsulfanyl-imidazo[2,1- b]thiazol-5-yl)-
30	2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
	\

	$\sqrt{3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4}$
	hydroxy-6-methyl-pyran-2-one;
	3-[7(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
5	3-[7-(2,4 dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]
=- 1	4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;
Sub.	4-hydroxy-o-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7
All	tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
•	3-[7-(5-chloro-1-methyl-3-phenyl-1H-pyrazol-4-yl)-2,3,6,7-tetrahydro
_ 10	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
1	3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3 <i>H</i> -benzo[<i>b</i>][1,4]diazepin-2
	yl]-4-hydroxy-6-methyl-pyran-2-one;
	3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4
	hydroxy-6-methyl-pyran-2-one;
	3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4
a 15 □ 	hydroxy-1 <i>H</i> -quinolin-2-one;
-	4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-
	[1,4]thiazepin-5-yl]-pyran-2-one;
	3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]
20	4-hydroxy-6-methyl-pyran-2-one;
	3-[7-(4-dimethylamino-2-methoxy\phenyl)-2,3,6,7-tetrahydro-
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2 one;
	3-hydroxy-2-[2-(2,4-diethoxy-henyl)-2,3-dihydro-
	benzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone;
25	$3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1H-1\lambda^4-$
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one
	10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-\0H-2,5-dioxa-9-thia-
	6a-aza-cyclohepta[a]naphthalene-1,6-dione;
	3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1 H -1 λ^6 -
30	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	· ·

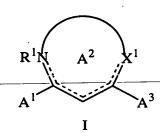
3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-

methyl-pyran-2-one; 3-(7-[2,2']\text{\text{hitenyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-} methyl-pyran-2-one; 5 2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxycyclohex-2-enone; and 3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6methyl-5,6-dihydro-pyran-2-one; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt 10 Ū thereof. m A method of treating a disorder responsive to the induction of 64. apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound selected from the group consisting of: 4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran\2-one; 3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; 3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; 3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one; 3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-25 hydroxy-6-methyl-pyran-2-one; 3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; 6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

	6-methyl-3-(2-p-tolyl-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl)
	pyran-2-one;
	4-hydroxy 6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro
	benzo[b][1,4]thiazepin-4-yl]-pyran-2-one; and
5	3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-
	6-methyl-pyran-2-one;
Subj	4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-
61	[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and
07	4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
_ 10	yl]-6-methyl-pyran-2-one; or
	a N-oxide derivative, prodrug derivative, protected derivative, individual
151 151	stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt
	thereof.
5	65. The method of claim 64, wherein said compound is selected from
9 15 4 0 0	the group consisting of:
<u>l.</u> Ti	4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-
Management of the state of the	[1,4]thiazepin-5-yl]-pyran-2-one;
<u> </u>	3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-
	4-hydroxy-6-methyl-pyran-2-one; and
20	6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-
	[1,4]thiazepin-5-yl]-pyran-2-one; or
	a N-oxide derivative, prodrug derivative, protected derivative, individual
	stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt
	thereof.
25	66. A method for treating or preventing cancer, comprising

administering to an animal in need of such treatment an effective amount of a

compound of Formula I:



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in which:

the dashed lines indicate optional unsaturation without violating valency rules;

 R^1 is hydrogen, (C_{1-6}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

 X^1 is -NR²-, -S-, S(O)-, -S(O)₂- or -O-, wherein R² is hydrogen or (C_{1-6}) alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom;

A¹ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A¹ together with R1 and the atoms to which A1 and R1 are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A¹ may be substituted with a group selected from -R³, -X²OR³, -X²C(O)R³, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(Q)_2NR^3R^4$, wherein X^2 is a bond or (C₁₋₆)alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo substituted (C_{1-6}) alkyl, wherein each ring within A1 and R5 contains from 3 to 8 ring atoms and may be

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substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^{2}NR^{4}C(O)OR^{4}$, $-X^{2}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{4})NR^{4}R^{4}$, -X2NR4S(O)2R6 and -X2S(O)2NR4R4, wherein X2 and R4 are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A1 and R5 may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the provisos that only one of A1 and R5 is a fused polycyclic ring system;

A² is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A² may be substituted with a group selected $from -R^8, -X^2OR^8, -X^2C(O)R^8, -X^2OC(O)R^8, -X^2C(O)OR^8, -X^2SR^8, -X^2S(O)R^8, -X^2S(O)R$ $-X^{2}S(O)_{2}R^{8}$, $-X^{2}NR^{4}R^{8}$, $-X^{2}NR^{4}C(O)R^{8}$, $-X^{2}NR^{4}C(O)OR^{8}$, $-X^{2}C(O)NR^{4}R^{8}$, $-X^2NR^4C(O)NR^4R^8, -X^2NR^4C(NR^4)NR^4R^8, -X^2NR^4S(O)_2R^8 \ and \ -X^2S(O)_2NR^4R^8, -X^2NR^4C(O)_2R^8 \ and \ -X^2S(O)_2NR^4R^8, -X^2NR^4C(O)_2NR^4R^8, -X^2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_2NR^4C(O)_$ wherein X^2 is a bond or (C_{1-6}) alkylene, R^8 is $-X^2$ R^9 wherein X^2 is as defined above and R9 is aryl containing a total of 6 to 10 ring\atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6, -X^2OC(O)R^6, -X^2C(O)OR^4, -X^2SR^4, -X^2S(Q)R^6, -X^2S(O)_2R^6, -X^2S(O)_2R^6,$ $-X^{2}NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)R^{6}$, $-X^{2}NR^{4}C(O)OR^{4}$, $-X^{2}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{4})NR^{4}R^{4}$, $-X^{2}C(O)NR^{4}X^{2}C(O)OR^{4}$, -X2NR4S(O)2R6 and -X2S(O)2NR4R4, wherein X2 and R4 are as defined above and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from

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 (C_{16}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

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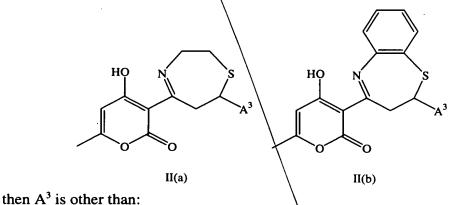
A is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and ansaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from -R9, -X2OR9, -X2C(O)R9, -X2OC(O)R9, $-X^2C(O)OR^9$, $-X^2SR^9$, $X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6}) alkylene, R^9 is -X²R¹⁰ wherein X² is as defined above and R¹⁰ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A³ and R¹⁰ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C₁₋₆)alkyl, cyano, halo, nitro, halo-substituted (C_{1.6})alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^{2}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{\lambda})NR^{4}R^{4}$, $-X^{2}NR^{4}S(O)_{2}R^{6}$ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R⁶ is (C_{1.6})alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A³ and R¹⁰ may be substituted further with 1 to 2 groups independently selected from (C_{1.6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A³ and R¹⁰ is a fused polycyclic\ring system; or an N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula $\dot{\mathbf{I}}(\mathbf{a})$:

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then A³ is other than:

- (a) \benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.
- 67. The method of claim 66, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



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A is outer than.

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

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68. The method of claim 66, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):

then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) 2,3-dihydro-benzo[1,4]dioxinyl; and
- (c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C_{1-3}) alkyl; or

a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof..

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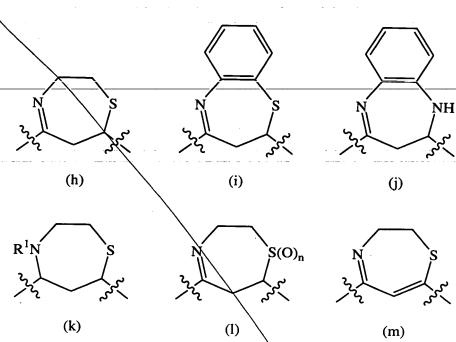
69. The method of Claim 66, wherein A of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 , or

A² and A¹ together with R¹ and the atoms to which A¹ and R¹ are attached forms a group of Formula (g):

wherein X¹ is -S- and the free valance is attached to A³; and

A² of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



in which n is 1 or 2 and R¹ is acetyl or trifluoroacetyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

- The method of Claim 69, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, halo, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and R^6 is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and (C_{1-6}) alkyl or halo-substituted derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.
- 71. The method of Claim 70, wherein said compound is selected from the group consisting of:

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4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; 2-[7\(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; 4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; 3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one; 3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-10 0 0 0 0 0 0 4 0 4 4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; 3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; 2-[7-(2,4-diethoxy-phen)])-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; _{*} 15 3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone; 3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-Ī benzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone; 4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one; 20 4-hydroxy-6-methy1-3-[7-(2,3,4-trimethoxy-pheny1)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyrah-2-one; and 3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazenin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; or 25 a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

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72. The method of claim 66, wherein said compound is selected from the list consisting of:

	3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-
	methyl-pyran-2-one;
	3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-
	5-yl]-4-hydroxy-6-methyl-pyran-2-one;
5	1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-
שיים פול	[1,4]thizepan-4-yl]-ethanone;
13	4-hydroxy-6-methyl-3-[7-(3-phenyl-1H-pyrazol-4-yl)-2,3,6,7-tetrahydro-
H	[1,4]thiazepin-5-yl]-pyran-2-one;
	3-[7-(5-ethyl-thien 2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
_10 	hydroxy-6-methyl-pyran-2-one;
	3-[7-(1-benzyl-1 <i>H</i> -indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
<u>L</u>	hydroxy-6-methyl-pyran-2-one;
J.	4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-
T T T	tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
= 15	4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-
£	tetrahydro-[1,4]thiazepin-5-yl]-pyran-2\one;
- 	4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-
	tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
	4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-
20	tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; \setminus
	3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-
	5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-
	5-yl]-4-hydroxy-6-methyl-pyran-2-one;
25	4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-
	2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;
	3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
	yl}-4-hydroxy-6-methyl-pyran-2-one;
	3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
30	yl}-4-hydroxy-6-methyl-pyran-2-one;

1	3-{\frac{1}{2}-(4-\text{circle}) - \text{circle} - circl
	yl}-4-hydroxy-6-methyl-pyran-2-one;
	4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2
	yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;
5	3-[7-(4-\formo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4
<u></u>	hydroxy-6-methyl-pyran-2-one;
500	3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4
AG	hydroxy-6-methyl-pyran-2-one;
	3-[7-(1-benzenesulfonyl-1H-pyrrol-2-yl)-2,3,6,7-tetrahydro
_10	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
Ţ	4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro
10 Lj	[1,4]thiazepin-5-yl]-pyran-2\one;
	4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro
	[1,4]thiazepin-5-yl]-pyran-2-one;
[™] 15	4-hydroxy-6-methyl-3- $[7]$ (1-methyl-1 H -indol-3-yl)-2,3,6,7-tetrahydro
	[1,4]thiazepin-5-yl]-pyran-2-one;
C 4 5 5	3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1H-pyrazol-4-yl)-2,3,6,7
	tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1H-pyrrrol-2-yl]-2,3,6,7
20	tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;
	3-(7-[2,2']bithienyl-5-yl-2,3,6,7 tetrahydro-[1,4]thiazepin-5-yl)-4
	hydroxy-6-methyl-pyran-2-one;
	3-{7-[1-(3,5-dichloro-phenyl)-1H-pyrrrol-2-yl]-2,3,6,7-tetrahydro
	[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;
25	$3-\{7-[1-(4-chloro-phenyl)-1H-pyrrol-2-yl]-2,3,6,7-tetrahydro$
	[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;
	3-[7-(5-chloro-1 <i>H</i> -indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4
	hydroxy-6-methyl-pyran-2-one;
	4-hydroxy-6-methyl-3-[7-(6-p-tolylsulfanyl-imidazo[2,1-b]thiazol-5-yl)
30	2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

	3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
	hydroxy-6-methyl-pyran-2-one;
	3\[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-
	[1,4]thiazenin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
5	3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-
	4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;
b	4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-
$\sqrt{3}$	tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;
ł '	3-[7-(5-chloro-1-methyl-3-phenyl-1 <i>H</i> -pyrazol-4-yl)-2,3,6,7-tetrahydro-
_10	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
<u> </u>	3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3H-
jj Jj	benzo[b][1,4]diazepin-2-yl 4-hydroxy-6-methyl-pyran-2-one;
	3-[7-(4-dimethylaminophenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
	hydroxy-6-methyl-pyran-2-one;
15	3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
	hydroxy-1 <i>H</i> -quinolin-2-one;
	4-hydroxy-6-methyl-3-[7-(4-thifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-
## ##	[1,4]thiazepin-5-yl]-pyran-2-one;
-	3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-
20	4-hydroxy-6-methyl-pyran-2-one;
	3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-
	benzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone
25	$3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1H-1\lambda^4-$
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;
	10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10 <i>H</i> -2,5-dioxa-9-thia-
	6a-aza-cyclohepta[a]naphthalene-1,6-dione;
	$3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3)$ 6,7-tetrahydro-1 H -1 λ^6 -
30	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

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4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-pyran-2-one;

4-hydroxy 3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

74. The method of claim 73, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl 3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

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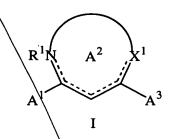
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75. The method of Claims 66 and 73, wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides,

head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer an prostatic carcinoma.

76. A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

 R^1 is hydrogen, (C_{1-6}) alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R is as defined below;

 X^1 is -NR²-, -S-, -S(O)-, -S(O)₂- or -O-, wherein R² is hydrogen or (C₁₋₆)alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom.

A¹ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A¹ together with R¹ and the atoms to which A¹ and R¹ are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A¹

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may be substituted with a group selected from -R³, -X²OR³, -X²C(O)R³, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C₁₋₆)alkylene, R³ is -X²R⁵ wherein X² is as defined above and R⁵ is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R⁴ at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, wherein each ring within A¹ and R⁵ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1.6})alkyl, cyano, halo, nitro, halo-substituted (C_{1.6})alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, $-X^2C(O)OR^4, -X^2SR^4, -X^2S(O)R^6, -X^2S(O)_2R^6, -X^2NR^4R^4, -X^2NR^4C(O)R^6, -X^2NR^4R^4, -X^2NR^4C(O)R^6, -X^2NR^4R^4, -X^2N^4R^4, -X^2N^4R^4, -X^2N^4R^4, -X^2N^4R^4, -X^2N^4R^4, -X^2N^4R^4, -X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, -X²NR⁴S(O)₂R⁶ and -X²S(O)₂NR⁴R⁴, wherein X² and R⁴ are as defined above and R^6 is $(C_{1.6})$ alkyl or halo-substituted $(C_{1.6})$ alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A1 and R5 may be substituted further with 1 to 2 groups independently selected from (C₁₋₆)alkylidene, oxo, imino and thioxo, with the provisos that only one of A¹ and R⁵ is a fused polycyclic ring system;

from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)O^2R^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X2 is a bond or (C1-6) alkylene, R8 is -X2R9 wherein X2 is as defined above and R9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a

A² is a monocyclic or fused bicyclic ring selected from heteroarylene or

unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A² may be substituted with a group selected

total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R4 at each occurrence independently is hydrogen, (C1-6)alkyl or

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halo-substituted (C₁₋₆)alkyl, wherein each ring within A² and R⁸ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C_{1-6}) alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4R^{\lambda}$ $-X^{2}NR^{4}C(O)NR^{4}R^{4}$, $-X^{2}NR^{4}C(NR^{4})NR^{4}R^{4}$, $-X^{2}C(O)NR^{4}X^{2}C(O)OR^{4}$, -X2NR4S(O)2R6 and -X2S(O)2NR4R4, wherein X2 and R4 are as defined above and R⁶ is (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6}) alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R⁸ is a fused polycyclic ring system; and

A³ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A³ may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9, -X^2SR^9, -X^2S(O)R^9, -X^2S(O)_2R^9, -X^2NR^4R^9, -X^2NR^4C(O)R^9,$ $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^{\flat} is a bond or (C_{1-6}) alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R4 at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted (C₁₋₆)alkyl, wherein each ring within A³ and R¹⁰ contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, cyano, halo, nitro, halo-substituted (C₁₋₆)alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{16}) alkyl or

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halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^3 and R^{10} is a fused polycyclic ring system; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.; with the proviso that when said compound is of Formula II(a):

then A³ is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.
- 77. The method of claim 76, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):

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then A³ is other than:

- benzo[1,3]dioxolyl; (a)
- phenyl which is mono-substituted by bromo, nitro, hydroxy, (b) methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.
- 78. The method of claim 76, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):

then A^3 is other than:

- (a) benzo[1,3]dioxolyl;
- 2,3-dihydro-benzo[1,4]dioxinyl; and (b)

79. The method of Claim 76, wherein A¹ of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6}) alkyl and the free valance is attached to A^2 , or

A² and A¹ together with R¹ and the atoms to which A¹ and R¹ are attached forms a group of Formula (g):

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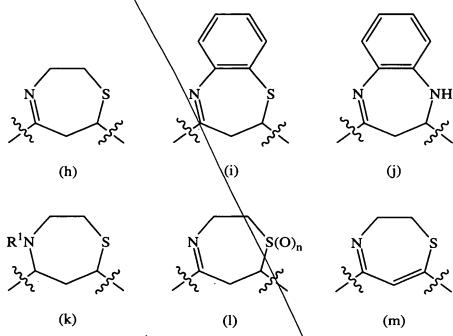
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wherein X¹ is -S- and the free valance is attached to A³; and

A² of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



in which n is 1 or 2 and R¹ is acetyl or trifluoroacetyl; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

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80. The method of Claim 79, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$,

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wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6}) alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6}) alkyl, halo, halo-substituted (C_{1-6}) alkyl, $-X^2CR^4$, $-X^2CR^4$, $-X^2CCR^4$, $-X^2CCR^4$, $-X^2CCR^4$, halo-substituted occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl and CC_{1-6} alkyl or halo-substituted (C_{1-6}) alkyl and CC_{1-6} alkyl or halo-substituted (C_{1-6}) alkyl or halo-substituted derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

81. The method of Claim 80, wherein said compound is selected from the group consisting of:

4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclonex-2-enone;

4-hydroxy\3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1;4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone

3-hydroxy-2-[2-(2,3,4-tri\methoxy-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

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4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; or

a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

82. The method of claim 76, wherein said compound is selected from the list consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2 tone;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)[1,4]thizepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

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	3 [7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-
	5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-
	5-yl]-4-hydroxy-6-methyl-pyran-2-one;
5	4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-
.	2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;
M	3-{7-[5-(2-chlorophenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
A15	yl}-4-hydroxy-6-methyl-pyran-2-one;
14	3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
_10	yl}-4-hydroxy-6-methyl-pyran 2-one;
드 () () () () () () () () () () () () ()	3-{7-[5-(4-chloro-phenyl) furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-
Ø M	yl}-4-hydroxy-6-methyl-pyran-2-one;
	4-hydroxy-6-methyl-3-{7-[5-\2-chloro-5-trifluoromethyl-phenyl)-furan-2-
u: F	yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;
<u>U</u> 15	3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
	hydroxy-6-methyl-pyran-2-one;
F H C H	3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-
	hydroxy-6-methyl-pyran-2-one;
	3-[7-(1-benzenesulfonyl-1H-pyrrol-2-yl)-2,3,6,7-tetrahydro-
20	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2\one;
	4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-
	[1,4]thiazepin-5-yl]-pyran-2-one;
	4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-
	[1,4]thiazepin-5-yl]-pyran-2-one;
25	4-hydroxy-6-methyl-3- $[7-(1-\text{methyl-}1H-\text{indol-}3-\text{yl})-2,3,6,7-\text{tetrahydro-}$
	[1,4]thiazepin-5-yl]-pyran-2-one;
	3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1H-pyrazol-4-yl)-2,3,6,7-
	tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	$3-\{7-[1-(2,4-difluoro-benzenesulfonyl)-1H-pyrrro]-2-yl]-2,3,6,7-$
30	tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

hydroxy-6-methyl-pyran-2-one; $3-\{7-\{1-(3,5-dichloro-phenyl)-1H-pyrrrol-2-yl\}-2,3,6,7-tetrahydro-$ [1,4]thiazepin- 5_{7} yl $\}$ -4-hydroxy-6-methyl-pyran-2-one; 5 $3-\{7-[1-(4-chloro-phenyl)-1H-pyrrrol-2-yl]-2,3,6,7-tetrahydro-$ [1,4]thiazepin-5-yl}\(\frac{4}{4}\)-hydroxy-6-methyl-pyran-2-one; $3-[7-(5-\text{chloro-}\H-\text{indol-}3-\text{yl})-2,3,6,7-\text{tetrahydro-}[1,4]\text{thiazepin-}5-\text{yl}]-4$ hydroxy-6-methyl-pyran\2-one; 4-hydroxy-6-meth\\[-3-[7-(6-p-tolylsulfanyl-imidazo[2,1-b]thiazol-5-yl)-10 2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; OSOUTOTTO .. OTTOOL 3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4hydroxy-6-methyl-pyran-2-one; 3-[7-(2-chloro-5-trifludromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; 3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-5,6-dihydro-pyran-2\one; 4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; 3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-20 [1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; 3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3Hbenzo[b][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one; 3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4hydroxy-6-methyl-pyran-2-one; 25 3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[\(\)1,4]thiazepin-5-yl]-4hydroxy-1*H*-quinolin-2-one; 4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl), 2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; 3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-30 4-hydroxy-6-methyl-pyran-2-one;

•	3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro
	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;
	3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro
	benzo[b][1,4]thiazepin-4-yl]-cyclohex-2-enone;
5	$3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1H-1\lambda^4$
5M	[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;
	10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10H-2,5-dioxa-9-thia
A12	6a-aza-cyclohepta[a]naphthalene-1,6-dione;
	$3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1H-1\lambda^6$
10	[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran 2-one;
-	3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6
n	methyl-pyran-2-one;
	3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-
₩ 5 15	methyl-pyran-2-one;
1 5	2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-
	cyclohex-2-enone; and
	3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-
	methyl-5,6-dihydro-pyran-2-one; or
	a N-oxide derivative, prodrug derivative, protected derivative, individual
20	stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable sale
	thereof.
	83. A method for the treatment of drug resistant cancer, comprising

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83. A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one; $3\sqrt{7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4$ hydroxy-6\methyl-pyran-2-one; 3-[7(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; 6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-xl]-pyran-2-one; 6-methyl-3-(2-p-tolyl-2,3-dihydro-benzo[b][1,4]thiazepin-4-yl)pyran-2-one; 4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl]-pyran-2-one; 4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and 4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5yl]-6-methyl-pyran-2-one; or a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

84. The method of claim 83, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

85. The method of Claim 66, 73, 76 or 83, further comprising administering to said animal at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent.

- 86. The method of Claim 85, wherein said known cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin, Rituxan and alanosine
- 87. The method of Claim 66, 73, 75 or 83, further comprising treating said animal with radiation-therapy.
- 88. The method of Claim 66, 73, 76 or 83, wherein said compound is administered after surgical treatment for cancer.
- 89. The method of Claim 57, wherein said disorder is an autoimmune disease.
- 90. The method of Claim 57, wherein said disorder is rheumatoid arthritis.
- 91. The method of Claim 57, wherein said disorder is inflammation or inflammatory bowel disease.
 - 92. The method of Claim 57, wherein said disorder is psoriasis.
 - 93. The method of Claim 57, wherein said disorder is a skin disease.

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